

Substitute form 1448A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>  (use as many sheets as necessary)		Application Number	09/858,324
		Filing Date	8/23/01
		First Named Inventor	Underhill
		Group Art Unit	1614
		Examiner Name	Unknown
Sheet 1 of 4	Attorney Docket Number	3477.92	

U.S. PATENT DOCUMENTS						
Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number	Kind Code (if known)			
Sone	1	4,235,871		Papahadjopoulos et al.	11/25/80	
	2	4,762,915		Kung et al.	8/9/88	
	3	5,827,500		Demarchez et al.	10/27/98	
	4	5,877,207		Klein et al.	3/2/99	

FOREIGN PATENT DOCUMENTS								
Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T
		Office	Number	Kind Code (if known)				
Sone J	5	PCF WO	WO 98/08546		Institut National de la Sante et de la Recherche Medicale	3/5/98		N
	6	PCI WO	WO 99/24415		Institute of Medicinal Molecular Design, Inc.	5/20/99		N
	7	PCF WO	WO 99/33821		Allergan Sales, Inc.	7/8/99		N
	8	JP	10-114757		Shudo Koichi	5/6/98	Abstract	Y
	9	JP	10-114757		Shudo Koichi	5/6/98		N

OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS				
Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T	
Sone	10	Adams, Mark E., et al., <i>The role of viscosupplementation of hylan G-F 20 (Synvisc®) in the treatment of osteoarthritis of the knee: a Canadian multicenter trial comparing hylan G-F 20 alone, hylan G-F 20 with non-steroidal anti-inflammatory drugs (NSAIDs) and NSAIDs alone, Osteoarthritis and Cartilage, Vol. 213, pp. 213-228 (1995)</i>		
	11	Ahrens, Marion, et al., <i>Expression of Human Bone Morphogenetic Proteins-2 or -4 in Murine Mesenchymal Progenitor C3H10T½ Cells Induces Differentiation in to Distinct Mesenchymal Cell Lineages, DNA and Cell Biology, Vol. 12, No. 10, pp. 871-880 (1993)</i>		
	12	Amos, Brad, et al., <i>Retinoid-Sensitive Cells and Cell Lines, Methods in Enzymology, Vol. 190, pp. 217-225 (1990)</i>		
	13	Apfel, C., et al., <i>A retinoic acid receptor α antagonist selectively counteracts retinoic acid effects, Proc. Natl. Acad. Sci. USA, Vol. 89, pp. 7129-7133 (August 1992)</i>		
	14	Brunet, Lisa J., et al., <i>Noggin, Cartilage Morphogenesis, and Joint Formation in Mammalian Skeleton, Science, Vol. 280, pp. 1455-1457 (May 29, 1998)</i>		
	15	Capdevila, Javier, et al., <i>Endogenous and Ectopic Expression of noggin Suggests a Conserved Mechanism for Regulation of BMP Function during Limb and Somite Patterning, Developmental Biology, Vol. 197, pp. 205-217 (1998)</i>		
	16	Cash, David E., et al., <i>Retinoic Acid Receptor α Function in Vertebrate Limb Skeletogenesis: a Modulator of Chondrogenesis, The Journal of Cell Biology, Vol. 136, pp. 445-457 (January 27, 1997)</i>		
	17	Chambon, Pierre, <i>A decade of molecular biology of retinoic acid receptors, FASEB J., Vol. 10, pp. 940-954 (1996)</i>		
	18	Dollé, Pascal, et al., <i>Differential expression of genes encoding α, β and γ retinoic acid receptors and CRABP in the developing limbs of the mouse, Nature, Vol. 342, pp. 702-705 (December 7, 1989)</i>		
	19	Duke, Jackie, et al., <i>Effect of the Brachypod Mutation on Early Stages of Chondrogenesis in Mouse Embryonic Hind Limbs: An Ultrastructural Analysis, Teratology, Vol. 19, pp. 367-376 (1979)</i>		
	20	Duprez, D.M., et al., <i>Bone Morphogenetic Protein-2 (BMP-2) Inhibits Muscle Development and Promotes Cartilage Formation in Chick Limb Bud Cultures, Developmental Biology, Vol. 174, pp. 448-452 (1996)</i>		
	21	Duprez, Delphine, et al., <i>Overexpression of BMP-2 and BMP-4 alters the size and shape of developing skeletal elements in the chick limb, Mechanisms of Development, Vol. 57, pp. 145-157 (1996)</i>		
	22	Eckhardt, Karl, et al., <i>A retinoic acid receptor α antagonist counteracts retinoid teratogenicity in vitro and reduced incidence and/or severity of malformations in vivo, Toxicology Letters, Vol. 70, pp. 289-308 (1994)</i>		
✓	23	Eyrolles, Laurence, et al., <i>Retinobenzic Acids. 6. Retinoid Antagonists with a Heterocyclic Ring, J. Med. Chem., Vol. 37, pp. 1508-1517 (1994)</i>		

Substitute form 1448A/PTO		Complete if Known	
Examiner Signature	<i>Seimab Sone</i>	Date Considered	9/16/03

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 608. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

INFORMATION DISCLOSURE STATEMENT BY APPLICANT			Application Number	09/856,324
			Filing Date	8/23/01
			First Named Inventor	Underhill
			Group Art Unit	1614
			Examiner Name	Unknown
			Attorney Docket Number	3477.92
(use as many sheets as necessary)				
Sheet	2	of	4	
OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS (continued)				
24	Ghyselinck, Norbert B., et al., <i>Role of the retinoic acid receptor beta (RARβ) during mouse development</i> , <i>Int. J. Dev. Biol.</i> , Vol. 41, pp. 425-447 (1997)			
25	Giguere, Vincent, et al., <i>Identification of a receptor for the morphogen retinoic acid</i> , <i>Nature</i> , Vol. 330, pp. 624-629 (December 17, 1987)			
26	Hall, B.K., et al., <i>The membranous skeleton: the role of cell condensations in vertebrate skeletogenesis</i> , <i>Anatomy and Embryology</i> , Vol. 188, pp. 107-124 (1982)			
27	Hall, Brian K., et al., <i>Divide, accumulate, differentiate: cell condensation in skeletal development revisited</i> , <i>Int. J. Dev. Biol.</i> , Vol. 39, pp. 881-893 (1995)			
28	Hogan, Brigid L.M., <i>Bone morphogenetic proteins in development</i> , <i>Current Opinion in Genetics and Development</i> , Vol. 8, pp. 432-438 (1998)			
29	Ide, H., et al., <i>Retinoic Acid Promotes Proliferation and Chondrogenesis in the Distal Mesodermal Cells of Chick Limb Bud</i> , <i>Developmental Biology</i> , Vol. 130, pp. 767-773 (1988)			
30	International Search Report, International Application No. PCT/CA98/01106			
31	Jiang, Heng, et al., <i>Modulation of limb bud chondrogenesis by retinoic acid and retinoic acid receptors</i> , <i>Int. J. Dev. Biol.</i> , Vol. 39, pp. 617-627 (1995)			
32	Jones, C. Michael, et al., <i>Involvement of Bone Morphogenetic Protein-4 (BMP-4) and Vgr-1 in morphogenesis and neurogenesis in the mouse</i> , <i>Development</i> , Vol. 111, pp. 531-542 (1991)			
33	Kastner, Philippe, et al., <i>Vitamin A deficiency and mutations of RXRa, RXRβ and RARα lead to early differentiation of embryonic ventricular cardiomyocytes</i> , <i>Development</i> , Vol. 124, pp. 4749-4758 (1997)			
34	Keneko, Satoru, et al., <i>Retinoid Antagonists</i> , <i>Med. Chem. Res.</i> , Vol. 1, pp. 220-225 (1991)			
35	Kingsley, David M., et al., <i>The Mouse short ear Skeletal Morphogenesis Locus is Associated with Defects in a Bone Morphogenetic Member of the TGFβ Superfamily</i> , <i>Cell</i> , Vol. 71, pp. 399-410 (October 30, 1992)			
36	Kingsley, David M., <i>The TGF-β superfamily: new members, new receptors, and new genetic tests of function in different organisms</i> , <i>Genes &amp; Development</i> , Vol. 8, pp. 133-146 (1994)			
37	Kistler, Andreas, <i>Limb bud cell cultures for estimating the teratogenic potential of compounds; Validation of the test system with retinoids</i> , <i>Archives of Toxicology</i> , Vol. 60, pp. 403-414 (1987)			
38	Kochhar, D.M., <i>Limb Development in Mouse Embryos</i> , <i>Teratology</i> , Vol. 7, pp. 289-298 (1973)			
39	Kochhar, Devendra M., et al., <i>The use of a retinoid receptor antagonist in a new model to study vitamin A-dependent developmental events</i> , <i>Int. J. Dev. Biol.</i> , Vol. 42, pp. 601-608 (1998)			
40	Koyama, E., et al., <i>Retinoids and Their Nuclear Receptors Promote the Completion of Chondrocyte Maturation During Limb Skeletogenesis</i> , <i>Abstract, Chondrogenesis and Osteogenesis</i> , pp. 71a			
41	Koyama, Eiki, et al., <i>Retinoid Signaling is Required for Chondrocyte Maturation and Endochondral Bone Formation during Limb Skeletogenesis</i> , <i>Developmental Biology</i> , Vol. 208, pp. 375-391 (1999)			
42	Kwasigroch, T.E., et al., <i>Production of Congenital Limb Defects with Retinoic Acid: Phenomenological Evidence of Progressive Differentiation During Limb Morphogenesis</i> , <i>Anat. Embryol.</i> , Vol. 181, pp. 105-113 (1980)			
43	Lee, Kenneth K.H., et al., <i>Influence of Digits, Ectoderm, and Retinoic Acid on Chondrogenesis by Mouse Interdigital Mesoderm in Culture</i> , <i>Developmental Dynamics</i> , Vol. 201, pp. 297-309 (1994)			
44	Lohnes, David, et al., <i>Function of Retinoic Acid Receptor γ in the Mouse</i> , <i>Cell</i> , Vol. 73, pp. 643-658 (May 21, 1993)			
45	Lohnes, David, et al., <i>Function of the retinoic acid receptors (RARs) during development (I) Craniofacial and skeletal abnormalities in RAR double mutants</i> , <i>Development</i> , Vol. 120, pp. 2723-2748 (1994)			
46	Lufkin, Thomas, et al., <i>High postnatal lethality and testis degeneration in retinoic acid receptor α mutant mice</i> , <i>Proc. Natl. Acad. Sci. USA</i> , Vol. 90, pp. 7225-7229 (August 1993)			
47	Luo, Guangbin, et al., <i>BMP-7 is an inducer of nephrogenesis, and is also required for eye development and skeletal patterning</i> , <i>Genes &amp; Development</i> , Vol. 9, pp. 2808-2820 (1995)			
48	Luo, Jiangming, et al., <i>Mice lacking all isoforms of retinoic acid receptor β develop normally and are susceptible to the teratogenic effects of retinoic acid</i> , <i>Mechanisms of Development</i> , Vol. 53, pp. 61-71 (1995)			
49	Lussier, Marc, et al., <i>Interdigital soft tissue separation induced by retinoic acid in mouse limbs cultured in vitro</i> , <i>Int. J. Dev. Biol.</i> , Vol. 37, pp. 555-564 (1993)			
50	Lyons, Karen M., et al., <i>Organogenesis and pattern formation in the mouse: RNA distribution patterns suggest a role for Bone Morphogenetic Protein-2A (BMP-2A)</i> , <i>Development</i> , Vol. 109, pp. 833-844 (1980)			
51	Macias, D., et al., <i>Role of BMP-2 and OP-1 (BMP-7) in programmed cell death and skeletogenesis during chick limb development</i> , <i>Development</i> , Vol. 124, pp. 1109-1117 (1997)			
52	Mangelsdorf, David J., et al., <i>The Retinoid Receptors</i> , <i>The Retinoids: Biology, Chemistry, and Medicine</i> , pp. 319-349 (1994)			
53	Marigo, Valeria, et al., <i>Sonic hedgehog Differentially Regulates Expression of FLI and GLI3 during Limb Development</i> , <i>Developmental Biology</i> , Vol. 180, pp. 273-283 (1996)			
Examiner Signature		Date Considered		
L. J. Noble		9/16/03		

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

Substitute form 1449A/PTO		Complete if Known	
<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		Application Number	09/856,324
(use as many sheets as necessary)		Filing Date	8/23/01
Sheet 3 of 4		First Named Inventor	Underhill
		Group Art Unit	1614
		Examiner Name	Unknown
		Attorney Docket Number	3477.92
<b>OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS (continued)</b>			
54	McBurney, M.W., et al., <i>Control of muscle and neuronal differentiation in a cultured embryonal carcinoma cell line</i> , <i>Nature</i> , Vol. 299, pp. 165-167 (September 9, 1982)		
55	Mendelsohn, C., et al., <i>Developmental analysis of the retinoic acid-inducible RAR-<math>\beta</math> promoter in transgenic animals</i> , <i>Development</i> , Vol. 113, pp. 723-734 (1991)		
56	Minas, Tom, et al., <i>Current Concepts in the Treatment of Articular Cartilage Defects</i> , <i>Orthopedics</i> , Vol. 20, pp. 525-538 (1997)		
57	Moses, Harold L., et al., <i>Regulation of differentiation by TGF-<math>\beta</math></i> , <i>Current Opinion in Genetics and Development</i> , Vol. 6, No. 5, pp. 581-8 (1996)		
58	Nuka, Satoshi, et al., <i>All-trans Retinoic Acid Inhibits Dexamethasone-induced ALP Activity and Mineralization in Human Osteoblastic Cell Line SV HFO</i> , <i>Cell Structure and Function</i> , Vol. 22, pp. 27-32 (1997)		
59	Paulsen, Douglas F., et al., <i>Stable, Position-Related Responses to Retinoic Acid by Chick Limb-Bud Mesenchymal Cells in Serum-Free Cultures</i> , <i>In Vitro Cell. Dev. Biol.</i> , Vol. 30A, pp. 181-186 (March 1994)		
60	Paulsen, Douglas F., et al., <i>Stage- and Region-Dependent Responses of Chick Wing-Bud Mesenchymal Cells to Retinoic Acid in Serum-Free Microcultures</i> , <i>Developmental Dynamics</i> , Vol. 201, pp. 310-323 (1994)		
61	Roark, Eileen F., et al., <i>Transforming Growth Factor-<math>\beta</math> and Bone Morphogenetic Protein-2 Act by Distinct Mechanisms to Promote Chick Limb Cartilage Differentiation in Vitro</i> , <i>Developmental Dynamics</i> , Vol. 200, pp. 103-118 (1994)		
62	Rosen, Vicki, et al., <i>Purification and Molecular Cloning of a Novel Group of BMPs and Locationization of BMP mRNA in Developing Bone</i> , <i>Connective Tissue Research</i> , Vol. 20, pp. 313-319 (1989)		
63	Rosen, Vicki, et al., <i>Signaling Pathways in Skeletal Formation: A Role for BMP Receptors</i> , <i>Annals New York Academy of Sciences</i> , Vol. 785, pp. 59-69 (1996)		
64	Ruberte, Esther, et al., <i>Specific spatial and temporal distribution of retinoic acid receptor gamma transcripts during mouse embryogenesis</i> , <i>Development</i> , Vol. 108, pp. 213-222 (1990)		
65	Sandell, Linda J., et al., <i>Alternative Splice Form of Type II Procollagen mRNA (IIA) is Predominant in Skeletal Precursors and Non-Cartilaginous Tissues During Early Mouse Development</i> , <i>Developmental Dynamics</i> , Vol. 199, pp. 129-140 (1994)		
66	Sandell, Linda J., et al., <i>Alternatively Spliced Type II Procollagen mRNAs Define Distinct Populations of Cells during Vertebral Development: Differential Expression of the Amino-Propeptide</i> , <i>The Journal of Cell Biology</i> , Vol. 114, No. 6, pp. 1307-1319		
67	Shenefelt, Ray E., <i>Morphogenesis of Malformations in Hamsters Caused by Retinoic Acid: Relation to Dose and Stage at Treatment</i> , <i>Teratology</i> , Vol. 5, pp. 103-118 (1972)		
68	Solloway, Mark, J., et al., <i>Mice Lacking Bmp6 Function</i> , <i>Developmental Genetics</i> , Vol. 22, pp. 321-339 (1998)		
69	Standeven, Andrew M., et al., <i>Retinoid-Induced Epiphyseal Plate Closure in Guinea Pigs</i> , <i>Fundamental and Applied Toxicology</i> , Vol. 34, pp. 91-98 (1996)		
70	Storm, Elaine E., et al., <i>Limb alterations in brachypodism mice due to mutations in a new member of the TGF<math>\beta</math>-superfamily</i> , <i>Nature</i> , Vol. 368, pp. 639-643 (April 14, 1994)		
71	Teng, M., et al., <i>Identification of highly potent retinoic acid receptor <math>\alpha</math>-selective antagonists</i> , <i>J. Med. Chem.</i> , Vol. 40, pp. 2445-2451 (1997)		
72	Underhill, T. Michael, et al., <i>Constitutively Active Retinoid Receptors Exhibit Interfamily and Intrafamily Promoter Specificity</i> , <i>Molecular Endocrinology</i> , Vol. 8, No. 3, pp. 274-285 (1994)		
73	Underhill, T. Michael, et al., <i>Retinoids and Their Receptors in Skeletal Development</i> , <i>Microscopy Research and Technique</i> , Vol. 43, pp. 137-155 (1998)		
74	Von Schroeder, Herbert P., <i>The Effects of Natural and Synthetic Retinoids on the Differentiation of RCJ C5.18 Chondrogenic Cells</i> , <i>Teratology</i> , Vol. 50, pp. 54-62 (1994)		
75	Wang, E. A., et al., <i>Bone Morphogenetic Protein-2 Causes Commitment and Differentiation in C3H10T1/2 and 3T3 Cells</i> , <i>Growth Factors</i> , Vol. 8, pp. 57-71 (1993)		
76	Winnier, Glenn, et al., <i>Bone morphogenetic protein-4 is required for mesoderm formation and patterning in the mouse</i> , <i>Genes &amp; Development</i> , Vol. 9, pp. 2105-2116 (1995)		
77	Wolpert, Lewis, <i>Signals in limb development: STOP, GO, STAY and POSITION</i> , <i>J. Cell Sci. Suppl.</i> , Vol. 13, pp. 199-208 (1990)		
78	Wozney, John M., et al., <i>Bone Morphogenetic Protein and Bone Morphogenetic Protein Gene Family in Bone Formation and Repair</i> , <i>Clinical Orthopaedics and Related Research</i> , Vol. 346, pp. 26-37 (1998)		
79	Yokouchi, Yuji, et al., <i>BMP-2/3 mediate programmed cell death in chicken limb buds</i> , <i>Development</i> , Vol. 122, pp. 3725-3734 (1996)		

Substitute form 1449A/PTO		Complete if Known	
Examiner Signature	<i>Loz...</i>	Application Number	09/856,324
		Date Considered	9/16/03

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.

<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b>		Filing Date	8/23/01
		First Named Inventor	Underhill
		Group Art Unit	1814
		Examiner Name	Unknown
		Attorney Docket Number	3477.92
(use as many sheets as necessary)			
Sheet	4	of	4
<b>OTHER PRIOR ART - NON PATENT LITERATURE DOCUMENTS (continued)</b>			
80	Yoshimura, Hiroyuki, et al., A Novel Type of Retinoic Acid Receptor Antagonist: Synthesis and Structure-Activity Relationships of Heterocyclic Ring-Containing Benzoic Acid Derivatives, <i>J. Med. Chem.</i> , Vol. 38, pp. 3163-3173 (1995)		
81	Zhang, Hongbing, et al., Mice deficient for BMP2 are nonviable and have defects in amnion/chorion and cardiac development, <i>Development</i> , Vol. 122, pp. 2977-2986 (1996)		
82	Zou, Hongyan, et al., Distinct roles of type I bone morphogenetic protein receptors in the formation and differentiation of cartilage, <i>Genes &amp; Development</i> , Vol. 11, pp. 2191-2203 (1997)		
83	Zou, Hongyan, et al., Requirement for BMP Signaling in Interdigital Apoptosis and Scale Formation, <i>Science</i> , Vol. 272, pp. 738-741 (May 3, 1996)		

Examiner Signature	<i>L. O. Nole</i>	Date Considered	9/16/03
--------------------	-------------------	-----------------	---------

\*EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to applicant.